Metabolic and Pubertal Alterations in Children with Narcolepsy-Cataplexy

Carine Villanueva, MD, PhD1, Caroline Verier-Weulersse, MD1, Aurore Guyon, PhD2,3, Marc Nicolino, MD, PhD4, Jian-Sheng Lin, MD, PhD5, Clara Odilia Inocente, DVM, PhD2,3, Patricia Franco, MD, PhD2,3

1Department of Pediatric Endocrinology, Hospices Civils de Lyon, Lyon, France
2Pediatrics Sleep Unit, Hospices Civils de Lyon, Lyon, France
3Unité de Recherche CNRS UMR5292, Université Lyon1, Lyon, France
4Department of Pediatrics, Children's Hospital of St. Louis, Washington University in St. Louis, St. Louis, MO, USA
5Institut Pasteur, Paris, France

INTRODUCTION AND HYPOTHESIS

Narcolepsy type 1 (also called hypocretin or orexin deficiency syndrome or narcolepsy with cataplexy) is a neurological disorder characterized by excessive daytime sleepiness, cataplexy (sudden loss of muscle tone triggered by emotions), hallucinations, sleep paralysis, impaired night-time sleep and short latency to rapid eye movement sleep after sleep onset. Narcolepsy Type 1 is caused by a deficiency of hypocretin neurons located in the dorso-lateral hypothalamus probably secondary to autoimmune destruction of hypocretin cells.

More than half of narcoleptic patients have an onset of symptoms prior to the age of 18 years. Narcolepsy in children is usually characterized by prominent sleepiness, more spontaneous than emotion-triggered cataplexy than in adulthood. Obesity has been reported in 30% of adult narcoleptic patients1,2, whereas it occurs in more than 50% of narcoleptic children with increasing body weight manifesting in the early course of the disease1.

More than 50% of adults with narcolepsy have metabolic syndrome. In children, obesity and metabolic abnormalities seem also to be more frequent. Precocious puberty has also been described in children with narcolepsy.

Objectives of our study: To study the effect of hypocretin deficiency on metabolic and pubertal characteristics in narcoleptic children. We compared the metabolic and pubertal alterations between 15 children with narcolepsy with cataplexy (narcolepsy type 1 or hypocretin deficient) and 15 control children matched for age, BMI z score.

Method:

Narcoleptic data were collected from the Reference Center for Narcolepsy and control common obese data from the department of pediatric endocrinology in Mother-Children’s Hospital in Lyon, France.

Narcoleptic patients underwent clinical interview, polysomnographic recordings, and human leukocyte antigen typing.

Height, weight, body mass index (BMI), waist circumference, arterial blood pressure and Tanner pubertal stage were evaluated in both children groups. Plasma lipid and glucose profiles were analyzed. For precocious puberty, plasma concentrations of hypothalamic-pituitary-gonadal axis hormones were determined.

CONCLUSION

BMI-independent metabolic and pubertal alterations in narcoleptic children suggest that hypocretin could modify the phenotype. A careful pubertal and metabolic follow-up of these patients is mandatory as well as tailored therapeutic management.

Results: metabolic syndrome

In this study, all the narcoleptic children had cataplexy, HLA DQB10602 and were obese. Both narcoleptic and obese control children were 11 years (5 to 17), 50% male, had a median BMI 26.3 kg/m2 (21 to 41) and BMI z score 3.6 SD (2.5 to 5).

<table>
<thead>
<tr>
<th></th>
<th>age</th>
<th>BMI</th>
<th>BMI z score</th>
<th>HOMA-IR</th>
<th>HbA1C</th>
<th>Striatosis</th>
<th>Advanced or precocious puberty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obese boys</td>
<td></td>
<td>11.0</td>
<td>26.3 (20.3-41.1)</td>
<td>3.5</td>
<td>1.6</td>
<td>5.4 (4.5-5.9)</td>
<td>1/15</td>
</tr>
<tr>
<td>Obese girls</td>
<td></td>
<td>11.0</td>
<td>26.3 (20.3-41.1)</td>
<td>3.6</td>
<td>2.3</td>
<td>5.6 (5.1-5.8)</td>
<td>8/15</td>
</tr>
</tbody>
</table>


Results: Puberty

- In the narcoleptic group: 2 girls and one boy have advanced puberty and 3 girls and 2 boys have precocious puberty.
- In the common obese children group: only one girl and one boy have advanced puberty (NS), none had precocious puberty (p=0.02).
- Cerebral and hypothalamic pituitary region MRI were normal in both cases.

Discussion

- For children with narcolepsy, the loss of orexin neurons could be associated with other hypothalamic anomalies.
- Obesity + metabolic syndrome and precocious puberty are frequently found in narcoleptic children.
- Complexity of all of these symptoms requires a multidisciplinary approach
- Need controlled studies to then evaluate the multidisciplinary follow and the treatment efficiency.

*The authors declare no conflicts of interest